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Opportunities and obstacles in translating evidence to policy in occupational asthma

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Abstract

Purpose—Occupational asthma (OA), a common respiratory disorder in Western countries, is caused by exposures at the workplace. It is part of a broader definition of work-related asthma (WRA) that also includes pre-existing asthma aggravated by substances present in the workplace environment, and it is potentially preventable. The purpose of this paper is to illustrate preventive measures for occupational asthma by case studies.

Methods—In three case studies we discuss preventive measures that have been associated with reductions in incidence of occupational asthma from natural rubber latex and from diisocyanates as supported by published literature. We also discuss challenges in relation to asthma from cleaning products in healthcare work.

Results and conclusions—Several preventive measures have been associated with reduction in incidence of occupational asthma from natural rubber latex and from diisocyanates, and may provide lessons for prevention of other causes of occupational asthma. Cleaning products remain an unresolved problem at present with respect to asthma risks but potential measures include the use of safer products and safer applications such as avoidance of spray products, use of occupational hygiene methods such as improving local ventilation, and when appropriate, the use of personal protective devices.

Keywords

Work-related asthma; Occupational asthma; Natural rubber latex; Diisocyanates; Cleaning agents

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Introduction

Worldwide, occupational health risk accounts for almost 2% of the burden of disease in terms of disability-adjusted life years [1]. Respiratory hazards can be present at worksites in the form of dust, fumes, gases, or volatile organic compounds. Occupational asthma (OA), a common respiratory disorder in Western countries, is caused by exposures at the workplace. It is part of a broader definition of work-related asthma (WRA) that also includes pre-existing asthma aggravated by substances present in the workplace environment [2]. Most OA results from an immunological response to workplace agents [3]. The prevalence of WRA ranges from 4% to 23%, depending on the case definition [4,5]. Approximately 18% of all adult-onset asthma is attributed to work-related exposures [6] indicating that the burden of OA is substantial on workers' health. This is especially important since many of the workplace exposures, of which more than 400 have been linked to OA [7], are preventable.

Prevention is a hallmark of epidemiology. Epidemiologic studies play a vital role in identifying high-risk populations through surveillance activities, providing evidence for an exposure-response relationship using etiologic studies, and evaluating efficacy, effectiveness, and efficiency through the use of interventions. Results from these studies serve as a basis for developing workplace health-related policies and regulations. Randomized controlled studies provide much stronger evidence in support of primary prevention efforts as they are less prone to selection bias and confounding. However, these are not common in occupational asthma research [8]. Hence, much evidence on the exposure-response relationship and workplace reduction of exposures in occupational asthma research comes from nonrandomized, clinical, and observational epidemiological studies.

This case study examines how epidemiological evidence helped shape policies to reduce worksite exposure to natural rubber latex and diisocyanates to prevent occupational asthma. Examples are given of epidemiologic studies that collectively provided information that contributed to the introduction of preventive measures. The case study then examines emerging evidence on the association of exposure to cleaning substances with occupational asthma in health care workers.

The three examples presented in this case study carry some different messages. The first example, of natural rubber latex (NRL), shows how the introduction of one policy (universal precautions) can result in a different problem (NRL allergy). This included risks of NRL allergy among workers who adopted the use of NRL glove use when they were at low risk for transmissible disease. The second example, of diisocyanate sensitization, illustrates how new policies may need to address heterogeneity in risk effects and can target different levels of prevention (primary, secondary, and tertiary prevention). The third case example illustrates the need for policies to balance competing risks (infections from health care facilities vs. risks of asthma). The "lessons learned" section relates to *challenges* of translating evidence into policy.

Case study #1: natural rubber latex-induced asthma

Background

NRL is manufactured from milky fluid or sap derived from the rubber tree *Hevea brasiliensis*, that is comprised of several different proteins [9,10]. Antioxidants, accelerators, casein, and starch are added to NRL to obtain desired strength, stretch, and durability properties [10,11]. Liquefied NRL is used in the manufacturing of many industrial, medical, and household products, including latex gloves [11]. Occupations that commonly involve exposure to NRL-containing products include health care professionals, hairdressers, food service workers, housekeepers, and workers in latex manufacturing [12].

NRL gloves have been the most widely used form of NRL products, especially in health care [11]. The types and their patterns of use have evolved over the past 20 years, based in part on reports of adverse health effects that led to changes in policies and regulations worldwide. These included more stringent manufacturing quality controls to decrease NRL allergenicity, less use of powdered latex gloves, and the availability of non-NRL glove alternatives.

NRL differs from synthetic rubbers in its ability to release proteins that can cause allergic reactions [9]. Three types of reactions can occur following exposure to a finished NRL product: IgE-mediated allergic reactions (type I), cell-mediated hypersensitivity (type IV), and contact irritation [12,13]. NRL allergy can cross-react with allergies to certain foods, such as bananas, avocados, and kiwis. Effects may be heightened in the presence of certain conditions such as spina bifida or other urogenital abnormalities [13].

The main routes of exposures to NRL are dermal and inhalation. IgE-mediated allergic reactions (Type I) are characterized by specific IgE antibodies in the body to proteins in natural latex [14]. IgE-mediated release of histamine and other mediators can cause urticaria or angioedema, allergic conjunctivitis, allergic rhinitis, asthma, and even anaphylaxis; events that can range from mild to life threatening [12–16].

In the 1980s and early 1990s, overall prevalence of latex sensitization among the general health care worker population was in the 3% to 5% range [17,18], although certain subgroups such as operating room staff had higher rates, closer to 6% to 10%. Van-denplas et al. [19] measured the proportion of latex-sensitized hospital workers who had latex-induced asthma confirmed by specific latex inhalation challenge, corresponding to about 2.5% of the hospital employees [17,19].

In 1992, the United States (U.S.) Occupational Safety and Health Administration (OSHA) passed the Bloodborne Pathogens Standard for the prevention of occupational HIV and hepatitis B transmission from needlesticks and other percutaneous exposures to blood. Central to the standard was a call for greater use of “universal precautions” (now called “standard precautions”) and personal protective equipment, leading to a major increase in latex glove use. The usage increased from 800 million pairs in the late 1980s to 4 billion in 1992, and up to 10 billion by 1996, making it difficult for American manufacturers to meet demand [11,20,21]. Gloves produced in other countries increased, resulting in an influx of gloves that at times were poorly produced and more allergenic. During the early 1990s,

reports of allergic reactions to NRL increased in the U.S. and worldwide [19,22–25]. The prevalence of sensitization appeared to be increasing, with studies reporting rates of over 10% [17,23,26]. Both the U.S. Food and Drug Administration (FDA) [27] and the National Institute for Occupational Safety and Health (NIOSH) [12] published alerts in 1997 expressing concern about the rise in latex-related allergic reactions, urging health care centers to develop and implement latex control policies, including the use of low-protein powder-free NRL gloves. This concern was echoed by a joint statement by the American Academy of Allergy, Asthma and Immunology and American College of Allergy, Asthma and Immunology [28]. Control recommendations also appeared more orless simultaneously in several countries, including the U.S., Germany, Finland, Italy, and Canada [17,22,29]. By 2000, following the introduction of powder-free/low-protein glove alternatives and other controls, the prevalence of sensitization had decreased from 10% to 4%–7% [30–32].

It is clear that NRL exposure has been a leading cause of OA, especially among health care workers using powdered latex gloves [33,34]. The overall incidence of NRL-induced OA peaked from 10.9 per 100,000 full-time equivalent health care workers in 1991 to 19.7 in 1998 [35]. However, along with the decreases in prevalence of NRL sensitization, this incidence later declined steadily to 3.8 per 100,000 in 2003–2004 [35], a trend confirmed by other studies. In 2001, Liss and Tarlo reported that the number of NRL-induced OA compensation claims among health care workers in Ontario decreased from 7 to 11 in 1991–1994 to 1–2 in 1997–1999 [15]. In 2007, a statewide survey of Texas health care workers reported a near doubling of the risk of new onset NRL-associated asthma in the period 1992 through 2000, but the risk disappeared after the year 2000, presumably due to widespread implementation of latex control policies [34]. Over this time period interventions varied and included nationwide policies and prevention programs, educational campaigns and training sessions, mainly focusing on the substitution with nonpowdered low-protein gloves, nonlatex devices, and institution-based early avoidance measures to prevent progression to severe disease [20,36].

The changes in policies over the 2 decades that involved chief local and government agencies including OSHA, FDA, and NIOSH led to an important publication by NIOSH, called the NIOSH alert: preventing allergic reactions to natural rubber latex in the work-place [12]. This publication offered recommendations to prevent NRL-related reactions in the workplace. These recommendations are currently followed throughout the U.S., consisting mainly of guidelines for better diagnosis of latex allergic reactions, combining clinical history, physical examination, pulmonary function tests where indicated and objective documentation of sensitization to latex, based on blood or skin-based testing. In addition to treatment of allergic/asthma symptoms with medications, special precautions for reducing allergy symptoms, while maintaining latex-safe areas in facilities were also recommended [12] (Table 1).

Managing NRL allergy centers on exposure control, following the industrial hygiene hierarchical approach of substitution, engineering controls, administrative controls, and use of personal protective equipment, along with worker and employer education. Most important is the elimination or reduction in use of powdered latex gloves [37]. Exposure-control recommendations were aimed at both employers and workers:

- For employers: providing nonlatex gloves to workers where infection potential is less, using only low-protein powder-free latex gloves when necessary, ensuring good housekeeping to remove latex-containing dusts, providing education programs and training material on latex allergy, implementing periodic screening, and evaluating current prevention strategies.
- For workers: using nonlatex gloves in activities not involving contact with infectious agents, appropriate barrier protection and use of power-free gloves with low-protein content, following appropriate work practices such as not using oil-based creams/lotions, washing hands with mild soap after glove use, and good housekeeping practices involving latex dust cleaning (carpets, upholstery, ventilation systems), taking advantage of allergy education and training involving identifi-cation of symptoms, avoiding direct contact with latex gloves and products, and consulting a physician when needed.

Evaluation of preventive measures

Although never legally mandated, hospitals in the U.S. and other countries began adopting many of these measures as of the mid-1990s, with associated decreases in both the incidence of symptoms associated with NRL allergy worldwide and in compensation claims [15,30,38,39]. Thus, in less than 20 years, the identifiscation and control of latex-related reactions serve as an example of successful translation of evidence into policy, with demonstrable decreases in NRL allergy rates, including asthma.

Case study #2: isocyanate-induced asthma

Background

Diisocyanates have been the most common chemical sensitizers causing OA in many industrialized areas [40–42]. They are low-molecular weight chemicals that are highly reactive due to the presence of two side chains of nitrogen, carbon, and oxygen, -N = C = 0. They are widely used in coatings, including spray paints as used for automotives, sealants for floors as well as adhesives. They are also used to produce flexible or rigid polyurethane foam, including spray foam insulation.

The oldest form of diisocyanates described to cause OA is toluene diisocyanate (TDI), a liquid that is volatile and therefore can be inhaled. Studies before 1980 reported annual incidence of OA among exposed workers up to 5%–8%, with prevalence rates above 10% [43], but rates have significantly fallen in more recent years in many countries such as the U.S., Canada, and European countries [40,44,45]. However, prevalence of OA up to 13.8% of exposed workers has recently been reported from Iran [46]. Other diiso-cyanates have been developed including the less volatile methylene diphenyl diisocyanate (MDI) which was hoped to have less risk of causing sensitization due to less inhalation. MDI is now the most commonly used diisocyanate in many areas. Despite lower volatility, there still is potential airborne exposure to workers in close proximity since it is heated or sprayed during use, or during activation, and in those settings risks of sensitization appear similar to risks from TDI [47]. This diisocyanate is widely used in adhesives, coatings, and spray foam insulation as well as in production of rigid polyurethane foam. An example of use as an

adhesive is in wood products such as medium density fiberboard and in oriented strand board: a layered combination of softwood with resin and MDI. In addition to the risks of sensitization from airborne exposure, it has also been suggested that skin exposure to MDI may cause sensitization and increase risk of developing OA after subsequent inhalation [47,48].

Other less commonly used diisocyanates include hexamethylene diisocyanate, and isophorone diisocyanate that is also volatile and may be found in spray paint. Relative risks of sensitization between various diisocyanates during occupational usage have not been clearly identified due to differences in usage and exposures, but it has been assumed that risks are greatest with TDI, less with MDI, and possibly less with polyisocyanates [49]. However, risks are also partly dependent on the extent of preventive measures as described later.

The mechanism of OA from diisocyanates remains incompletely understood but sensitization does appear to be mediated by immunologic mechanisms, and there are genetic markers that have been associated with OA from diisocyanates [50–53]. Specific IgE antibodies to diisocyanates linked to human albumin have been identified in up to 55% of patients with OA related to diisocyanates [54,55] and have been reported to be very specific for the diagnosis, although having relatively low sensitivity [56]. This suggests an IgE-associated allergic mechanism, at least for a large subset of those with OA from diisocyanates [57]. Support for an IgE-mediated response is also provided by anecdotal case reports of anaphylaxis related to diisocyanates. Lack of identified specific IgE antibodies in the remaining patients with OA from diisocyanates may be due to the lack of an appropriate antigen preparation for the test, or due to other immunologic mechanisms causing sensitization and activation of an inflammatory response. Specific IgG antibodies to diisocyanates linked to human albumin have been identified both in sensitized workers and in asymptomatic exposed workers and appear to be a marker of exposure rather than of OA [56]. However, their presence has also supported the clinical diagnosis of hypersensitivity pneumonitis, mainly from exposure to sprayed MDI [58].

Over the past several years, polyisocyanates have often been substituted for smaller diisocyanate molecules as hardeners in processes such as two-component adhesives and coatings. The assumption is that the combination of diisocyanates in larger molecules would reduce potential antigenicity compared with the equivalent number of reactive groups in smaller diisocyanate molecules, while maintaining the desired chemical activity [49].

Recommendations

Preventive measures for diisocyanate-induced OA

• Avoidance/reduction of exposure: These chemicals cannot easily be replaced at present. Less volatile diisocyanates such as MDI have increased in usage and the more volatile TDI has been in relatively reduced usage over the past few decades. Although MDI is often heated or sprayed, the use of this likely results in less inhaled exposure, especially in more open workplace areas. Polyisocyanates, expected to be less antigenic, have also been more widely substituted for the small diisocyanate molecules in recent years [49].

The risk of sensitization to diisocyanates is increased with higher exposures [59,60]. The following local preventive measures have therefore been advised to reduce respiratory exposure of workers: use of robots where possible in enclosed areas of expected higher exposures; occupational hygiene measures to improve ventilation in other areas of usage, and monitoring of workplace levels of diisocyanates, with legislated exposure limits; enclosure of areas containing diisocyanates such as separately ventilated booths for spray painting; as well as use of respiratory protective devices with appropriate filters such as use of air-supply respirators by workers performing spray painting [61]. Skin protection from exposure has also been advised as it may reduce risks of sensitization to diisocyanates [62].

Exposure limits have been established and continuous air monitoring to keep within allowable air concentrations has been mandated for workplaces using diisocyanates in some jurisdictions such as in the province of Ontario, Canada [63]. In the U.S., although there is no regulatory exposure limit for diisocyanates, a time-weighted average exposure limit of 0.005 ppm is recommended [64].

Occupational hygiene measures are also important in possible prevention of irritant-induced OA. Diisocyanates, in accidental high concentrations, can cause airway irritation and inflammation, resulting in irritant-induced asthma, so worker knowledge as to the appropriate action to take during an accidental spill of diisocyanates may prevent this outcome.

Although genetic factors have been associated with OA from diisocyanates, there are no current sensitive and specific markers that would justify the exclusion of particular individuals from work with diisocyanates. Workers with pre-existing asthma are not known to have an increased risk of becoming sensitized to diisocyanates, but due to the natural variability of asthma it may be more difficult to reach a diagnosis of OA in those workers.

• Secondary preventive measures: Medical surveillance has been advised for workers exposed to diisocyanates to detect sensitized workers relatively early and remove them from further exposure to improve their medical outcome [65]. Components include preplacement assessments with a respiratory questionnaire, and spirometry, and repeat of these at intervals during employment with diisocyanate exposure. An example of this was mandated in Ontario, Canada by the Ministry of Labor in 1983 [63]. It required preplacement performance as well as repeat of the questionnaire at least every 6 months and spirometry at least every year during the employment with diisocyanates. Development of respiratory symptoms or changes in spirometry from baseline would lead to a physician assessment to determine safety for that worker to continue in the same job. In Ontario, the introduction of this program was followed by an initial increase in workers' compensation allowed claims for diisocyanate-induced OA, consistent with increased case-finding ("Hawthorne effect"), followed by a sustained progressive drop in cases [40, 66]. While supportive of a benefit from medical surveillance, it is not possible to identify the specific component associated with benefit and other changes likely contributed to declines in OA rates during this time, such as the primary preventive measures discussed above, and a likely increase in worker knowledge of diisocyanates and asthma as mentioned below.

Although specific serum IgE and IgG antibodies to diisocyanates are not generally included currently in clinical medical surveillance programs for diisocyanates (due to relatively low sensitivity of specific IgE), it has been suggested that specific IgG antibodies could be used as a marker of worker exposure and of the effectiveness of exposure-control measures in a workplace [67].

- Worker education is a primary and secondary preventive measure that is often combined with a medical surveillance program. Knowledge of the risks of sensitization and of OA may enhance adherence to personal safety measures at work and encourage workers to seek early heath care assessment if respiratory symptoms occur [68].
- Physician education can also play a role in secondary and tertiary prevention. Improved knowledge of work-related asthma may lead to more targeted questioning of patients with respiratory symptoms regarding a work component, resulting in an earlier diagnosis [68].
- Tertiary preventive measures consist of appropriate management of workers who have developed OA from diisocyanates–including appropriate medications, removal from further exposure to diisocyanates, socioeconomic support via workers' compensation, and relocation to a different area in the same workplace or to another workplace (without exposure to dii-socyanates) [65].

Evaluation of preventive measures

Overall preventive measures (Table 2) have been successful in reducing OA from diisocyanates although it is difficult to determine the relative benefits of each measure. In Ontario, there were progressive declines in rates of workers' compensation claims accepted for diisocyanate-induced OA after 1990, following an initial increase consistent with greater case-finding after the medical surveillance measures were introduced [40,44,61]. There also was an earlier diagnosis after the medical surveillance was introduced (mean of 2 years from onset of symptoms vs. 3 years before the surveillance measures), with milder asthma at the time of diagnosis and a trend to better outcome [61]. However, in Ontario over time, there has also been an earlier diagnosis reached in nondiisocyanate OA claims, suggesting greater awareness by physicians and/or patients of WRA [61,66]. Falls in rates of diisocyanate-induced OA may also relate to the primary preventive measures: during the time when rates have fallen both in Ontario, Canada, and in other countries such as UK, and Belgium [45,69], there have been increases in use of MDI and polyisocyanates [49] rather than of TDI, more use of robotics in workplaces, and possibly better worker education and use of protective equipment.

Case study #3: cleaning and disinfecting in health care

Background

Cleaning and disinfecting are necessary activities in health care facilities, but they also have the potential to contribute to the onset and exacerbation of asthma and related respiratory symptoms. Unlike the other two topics addressed in this article, this topic involves different

agents with multiple mechanisms, and our understanding of these agents and related interventions is still under investigation.

Health care-associated infections (HAIs) pose a serious risk to the health of patients and workers, and are an ongoing challenge worldwide [70–72]. Environmental surfaces can become contaminated with pathogens from the hands of patients, workers, and visitors, these agents can remain or possibly increase in numbers without appropriate cleaning and/or disinfecting [73], and then be transferred to others [74,75]. Cleaning and/or disinfection can reduce the number of infectious agents on environmental surfaces in health care settings and lower the risk of infection [76,77]. Special attention to the cleaning and disinfection of a room previously occupied by an infected patient can reduce HAIs among subsequent occupants [78,79].

Common ingredients of cleaning and disinfecting products such as chlorine bleach, ammonia solutions, peracetic acid, and per-oxyacetic acid are irritants that can adversely impact the eyes, skin, and upper and lower airways of exposed workers. Irritant exposures like these have been identified as common causes of OA and work-exacerbated asthma among cleaners [80]. High-level accidental exposures to irritant gases can induce OA without latency, commonly called reactive airways dysfunction syndrome. In addition, chronic exposure to lower levels of irritants may result in asthma as well, although this remains under investigation [81]. With other disinfecting ingredients, sensitizing mechanisms are suspected but often only partially understood. From clinical studies, OA patients have had positive-specific inhalation challenge tests to agents such as quaternary ammonium compounds (quats), glutaraldehyde, ethanolamines, and ortho-phthalaldehydes, suggesting an immunologic response [82–84] though the exact mechanism is unclear [84–86].

There is a robust literature on the association of asthma with workplace exposure to cleaning and disinfecting products. These articles include case reports [84,87], as well as findings from surveillance [80,88] and epidemiologic studies conducted in general population samples [89] and among cleaning workers [90,91]. The findings from surveillance [92,93] and epidemiologic studies [34,94–98] support the conclusion that asthma and related symptoms are associated with cleaning and disinfecting activities in health care facilities. For example, a study of health care workers in France reported an association of current asthma with exposure to ammonia and to sprays with moderate/high intensity, with exposure based on both expert assessment and a job exposure matrix [97]. Participants with baseline asthma in the longitudinal Nurses' Health Study II in the United States were more likely to change to jobs that had lower exposure to disinfectants [98]. From an investigation of health care workers in Texas, onset of asthma after entering a health care profession was associated with job exposure matrix-assessed exposure to instrument cleaning and surface cleaning products [34,95,96], and work-related asthma symptoms and work-exacerbated asthma were associated with self-reported use of various cleaning and disinfecting products [94].

Preventive measures

In medical facilities, actions to protect health care workers from the harmful exposure to cleaning and disinfecting products are often judged by whether they compromise the goal of

infection prevention and control. As proposed recently by a working group in the United States, an integrated approach is needed, with the dual objective of preventing both HAIs and occupational illnesses in health care settings [99]. This approach is made possible by establishing a committee in which occupational safety and health staff engage directly with infection prevention staff, as well as with representatives of other stakeholders such as affected workers and management. The committee provides a framework for the selection, implementation, and monitoring of preventive practices. Members would meet regularly to assess the cleaning and disinfecting needs of the facility, identify the least hazardous chemical products and methods that will accomplish infection prevention goals, actively address employee health issues suspected to be caused by cleaning and disinfecting, and monitor the maintenance of cleaning/disinfecting and exposure-control equipment and the assessment of workplace exposures.

The following are descriptions of additional practices that support primary prevention, except where indicated as secondary prevention (Table 3).

- Substitution of a nonhazardous or less hazardous material is at the top of the hierarchy of controls in occupational environments [100]. Green chemistry holds the promise of cleaning and disinfecting products with fewer adverse health effects. However, the independent organizations that certify green products establish their own criteria, and there are no universally accepted criteria for green cleaners and disinfectants. An example of this are the Green Seal-37 criteria, which specify that industrial and institutional cleaning and disinfecting products should not include asthmagens and other harmful toxins [101]. The Green Seal organization defines an asthmagen as any asthma-causing agent that has fulfilled criteria for a sensitizer (other than enzymes) as determined by the Association of Occupational and Environmental Clinics in the United States [102]. It is unclear how widely green cleaning and disinfecting products are used in medical facilities, and whether they both prevent infections and do not contribute to respiratory problems among staff and patients. There have been instances in which a substitute product that prevents HAIs has an adverse health effect similar to the original product (such as when ortho-phthalaldehydes were used in place of glutaraldehyde) [83,103].
- Engineering controls such as isolation of the source of exposure and local exhaust ventilation are typically unrealistic with cleaning and disinfecting activities that are conducted in numerous dispersed locations throughout the workplace. However, some engineering controls can still be practical and effective in this setting. For example, the dilution of concentrated cleaning and disinfecting products can be automated in enclosed cabinets with exhaust ventilation that prevents worker exposure. Also, technological changes can potentially support infection control and limit exposure to chemical products. Spraying of cleaning products can contribute to aerosol exposures and has been associated with current asthma and related symptoms, both in health care and other settings [97,104]. Replacing spray products with wipes might reduce exposures and prevent some of the adverse respiratory effects. A promising

approach is to use materials like copper that have antibacterial properties in locations commonly touched by patients and staff, including door knobs, faucet handles, and patient over-bed tables [105]. These materials would likely reduce the need for chemicals to fight microbial agents. Nonchemical, nontouch approaches to terminal cleaning of vacated patient rooms and clinics, such as with ultraviolet light and hydrogen peroxide systems, hold promise and are still being investigated [106,107].

- Personal protective equipment (PPE) including respirators, gloves, protective clothing, and eye protection, are appropriate for some cleaning and disinfecting activities. Using respirators in a setting where patients and/or others are not protected may cause undo alarm. PPE use is feasible during terminal cleaning of patient or examination rooms in a medical center when patients and others are not present. However, this raises the issue of safe removal of gases, which might be re-circulated through a building's ventilation system, potentially exposing others who would not have PPE.
- Workers involved in cleaning and disinfecting need to be trained in proper use of different chemical products and equipment, and the use of PPE, consistent with their duties, to minimize exposure (primary prevention). Only a few ingredients of cleaning and disinfecting products (such as chlorine, ammonia, and 2-butoxyethanol) have received enough attention to warrant occupational exposure limits. However, manufacturers of cleaning and disinfecting products provide guidelines for proper use that should be communicated to workers. Workers should also be educated about possible health effects like respiratory symptoms to facilitate early recognition of disease (secondary prevention).

Lessons learned from the case studies

1. The history of NRL allergy and changes in glove use serve as an excellent example of how epidemiological research, government efforts, and community-based dissemination can effectively translate evidence into policies. Three main lessons emerge (Table 1). First, government agencies (FDA, NIOSH) played an important role in sentinel event detection, collection, and dissemination in the form of national alerts in raising awareness in the research and practice communities. This led to more rigorous epidemiological studies that confirmed the risk presented by occupational exposure to NRL. Second, the prompt elaboration of reasonable exposure-control recommendations led to their adoption by employers, usually on a voluntary basis, and was key to reducing disease incidence. And finally, research went beyond describing the problem and also evaluated the impact, albeit indirectly, of these control measures.
2. Interventions for diisocyanates (Table 2) may also be applicable to other sensitizing causes of OA. Some aspects of this model for other common sensitizing chemicals include the likely benefits of avoiding or minimizing worker skin and airborne exposures to sensitizers by substitution and occupational hygiene measures including use of robots when appropriate, use of protective equipment when avoidance is not possible; and consideration of a

medical surveillance program, when possible including tests for immunologic sensitization. Despite lack of clear evidence of the relative values of each of these measures, the approach to this common cause of OA can act as a model for other chemical sensitizers that cause OA and may be cost-effective [108].

3. Cleaning products remain an unresolved problem at present with respect to asthma risks but potential measures include the use of safer products and safer applications such as avoidance of spray products, use of occupational hygiene methods such as improving local ventilation, and when appropriate, the use of personal protective devices (Table 3).

Conclusions

Workplaces play an important role in creating jobs and driving economy. Therefore, it is no surprise that public policy makers and regulators in the U.S. have to address the concerns of a diverse group of stakeholders including businesses, industries, communities, and workers before coming up with policies acceptable to all the groups. Unfortunately, the process is painstakingly slow. No doubt workplaces are much safer today than 4 decades ago when OSHA was established through an act of Congress. Both fatal and non-fatal injuries and illnesses have declined substantially since 1971, but significant challenges remain. In 2015, the second and the fourth most frequently cited worksite standard violations related to chemical hazard communication and respiratory protection, respectively [109], two standards that are most relevant in reducing the occurrence of OA. Similarly, workplace regulatory exposure limits exists only for 470 chemical substances [110]; currently there are more than 85,000 chemicals listed in the Toxic Substances Control Act Chemical Substance Inventory [111]. Efforts by OSHA to reduce the exposure limits or regulate additional chemical exposures have met with challenges in courts by businesses and industries who argue regulations raise costs and undermine their economic interests. For worksite occupational health and safety programs to be successful, it requires organizational level changes such as removal of occupational hazards by substituting them with safer products, engineering controls like installing ventilation systems, training workers, and providing personal protective equipment if needed [112]. These system level changes are not possible without management support and addressing their concerns related to cost and benefit to their “bottom-line.” Epidemiology can help evaluate implementation of these programs, assess the effect of these system level changes on workers’ health, and identify savings in direct and indirect cost through cost-benefit and cost-effectiveness analysis. As illustrated in the examples of NRL and isocyanates, evidence based on clinical and epidemiological studies along with successful engagement of stakeholders led various organizations and employers to voluntarily adopt preventive measures to minimize workers exposure levels. A similar approach can be used to advance exposure reduction policy initiatives for cleaning-related chemicals.

Additional resources regarding cleaning agents

The report from the working group [99] previously mentioned includes additional observations about fulfilling the dual goal of infection and occupational illness prevention in health care, including research that would assist fulfilling this goal. Also, a professional

medical organization [113] recently provided suggestions for minimizing harmful exposures to cleaning and disinfecting agents. In terms of practical educational materials that can be used in workplaces, the U.S. government published a fact sheet in 2012 entitled “Protecting Workers Who Use Cleaning Chemicals” [114] that can be accessed online at http://www.cdc.gov/niosh/docs/2012-126/pdfs/2012-126.pdf.

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Table 1

Lessons learned from natural rubber latex

Preventive measures	Methods	
Primary preventive measures		
Avoidance/reduction of exposure	•	Change from latex gloves to powder free or nonlatex gloves
	•	Control exposure levels by removing latex-containing dusts
	•	Avoiding oil-based creams and lotions to prevent glove deterioration.
Secondary preventive measures		
Identifying sentinel events through surveillance	•	Government agencies such as the FDA and NIOSH played an important role in sentinel event detection, collection, and dissemination in the form of na- tional alerts that played an important role in raising awareness of NRL allergy in the research and practice communities. This led to more rigorous epidemiological studies that confirmed the risk presented by occupational exposure to NRL.
Worker education	•	Provide education and training to avoid (primary prevention) and early recognition (secondary prevention) of latex allergy symptoms.
Tertiary measures	•	Treatment of OA with medications, removal from further exposure, and providing support through workers compensation claims.

FDA = Food and Drug Administration; NIOSH = National Institute for Occupational Safety and Health; OA = occupational asthma.

Table 2

Lessons learned for OA from diisocyanates

Preventive measures	Methods
Primary preventive measures	
Avoidance/reduction of exposure	Change from diisocyanates to a nonsensitizing product Reduce usage Control exposure levels by occupational hygiene means such as containment, use of robots, improved ventilation Use of protective equipment–to reduce inhaled exposure, gloves, and coveralls to reduce skin exposure
Secondary preventive measures	
Medical surveillance has been advised for workers exposed to diisocyanates to detect sensitized workers relatively early and remove them from further exposure to improve their medical outcome [26].	Medical surveillance may include preplacement assessments including a respiratory questionnaire, and spirometry, and repeat of these at intervals during employment with diisocyanate exposure. Specific serum IgE when such tests are feasible, such as for enzymes, platinum salts, and high molecular weight sensitizers. It has been suggested that specific IgG antibodies could be used as a marker of worker exposure and of the effectiveness of exposure-control measures for diisocyanates.
Worker education	Worker education is a primary and secondary preventive measure often combined with a medical surveillance program. Knowledge of the risks of sensitization and of OA may enhance adherence to personal safety measures at work and encourage workers to seek early heath care assessment if respiratory symptoms occur [29].
Physician education	Physician education can also play a role in secondary and tertiary prevention. Improved knowledge of work-related asthma may lead to appropriate questioning of patients with respiratory symptoms regarding a work component, resulting in an earlier diagnosis.
Tertiary measures	Appropriate management of workers who have developed OA from diisocyanates–including appropriate medications, removal from further exposure to diisocyanates and socioeconomic support via workers' compensation and relocation to a different area in the same workplace or to another workplace (without exposure to diisocyanates)

OA = ccupational asthma.

Table 3

Proposed integrated approach to address cleaning and disinfecting in health care facilities

Preventive measures	Methods
Primary/secondary preventive measures	
Committee to address cleaning and disinfecting issues	• Establish the dual objective to prevent both health care-associated infections and occupational illnesses. • Pursue this objective by setting up a com- mittee with occupational safety and health staff, infection prevention staff, and other stakeholders (such as affected workers and management), to meet regularly and address issues related to cleaning and disinfecting.
Worker education	• Train workers in proper use of chemical products, equipment, and personal protec tive equipment, consistent with their cleaning and disinfecting duties, to minimize exposure (primary prevention). • Educate workers about possible health effects to facilitate early recognition of disease (secondary prevention).
Primary preventive measures	• Evaluate with input from stakeholders, and substitute nonhazardous or less hazardous products when possible. • Employ engineering controls when possible, such as diluting concentrated products in an enclosed ventilated system, avoiding use of sprayed products, and using materials like copper that have antibacterial properties in high-touch locations. • Use personal protective equipment such as respirators when appropriate.